

THE EFFICACY OF OXYTETRACYCLINE THERAPY AND THE DURATION OF TREATMENT IN THE COURSE OF BOVINE ANAPLASMOSIS

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SUMMARY

A total of 27 crossbred calves (12 intact, 9 splenectomised and 6 uninfected control) were subcutaneously inoculated with 2×10^7 *Anaplasma marginale* infected erythrocytes. Oxytetracycline (at 10mg/kg body weight) was administered intravenously when the PCV dropped to 16 per cent or below. The pattern of development of parasitaemia, appeared to be similar in both intact and splenectomised calves. The splenectomised calves, however, gave higher percentage of parasitaemia. Fluctuation in the PCV followed the same pattern in both groups, but the splenectomised calves were observed to suffer more anaemic crisis than the intact ones.

In the intact calves, all those treated once and for 2 consecutive days survived. In the splenectomised calves, all those treated once died, while all those treated for 2 consecutive days survived.

It may be concluded that, 2 consecutive oxytetracycline treatments (at 10mg/kg body weight) gave better recovery rates in cases of clinical bovine anaplasmosis.

INTRODUCTION

In Nigeria, Oxytetracycline is the drug widely used in the treatment of clinical anaplasmosis. The treatment regimen followed is based on the experience in other countries, such as the U.S.A. (Brock, 1959; Miller, 1956; Frankline *et al.* 1962), where conditions are different from those of Nigeria. Since it is probable that such regimen may not be valid under Nigerian conditions especially in relation to parasite strain and husbandry practice, it is important that an effective treatment be established in Nigeria based on control studies. In cattle, oxytetracycline is com-

monly used based on the manufacturer's commendation, of 10mg/kg body weight.

Apart from oxytetracycline, two other drugs, Imidocarb and Gloxazone, are now known to be efficacious in the therapy of anaplasmosis. Their use in Nigeria has been limited; while gloxazone has already been withdrawn from the market by the manufacturers due to toxicity problems.

Based on the foregoing, we studied the duration of therapy in bovine anaplasmosis in Nigeria, under controlled conditions, using oxytetracycline at 10mg/kg body weight.

MATERIALS AND METHODS

A total of 27 crossbred calves, obtained from the National Animal Production Research Institute's (NAPRI) farm were used. Their average age was 13.1 months (range 10—17 months). They were shown to be negative for *A. marginale* by microscopic examination and the rapid card agglutination test (Amerault and Roby, 1968; Amerault, 1973), after screening all the animals on the farm.

They were then randomly divided into 3 groups. Group A consisted of 12 intact calves; group B had 9 splenectomised calves, and group C 6 intact calves. Group C served as uninfected control. None of the splenectomised calves was used as control, because they may die of other infections apart from Anaplasmosis. All the

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animals in group A and B were later subdivided into 3 sub-groups based on the duration of treatment with oxytetracycline. Splenectomy was performed via a left paracostal laparotomy, using paravertebral anesthesia. Prior to inoculation with a carrier blood, for *A. marginale*, all the animals, especially the splenectomised ones, were kept under close observations for 14 days to exclude any other infections. The observations, included haematologic evaluation, microscopic examination of stained blood smears and daily rectal temperature. All the animals were found to be free of any blood parasites.

Infection and post-inoculation care: Two hundred millilitres (200ml.) of whole blood were collected from a selected donor which had previously been proved to be carrier of *A. marginale* (more than 0.1 per cent) by microscopic detection method and serologically by the rapid card agglutination test. The blood was collected in a sterile clean bottle containing 20ml. of 3 per cent Sodium Citrate Solution, as anticoagulant.

All the animals in groups A and B were each inoculated subcutaneously (s.c.) with 5ml. of the carrier blood, which gives approximately 2×10^7 *A. marginale* infected erythrocytes. Prior to and after inoculation, all the animals were kept in enclosed pens and were sprayed weekly with acaricide to prevent tick infestation. They were fed on silage and legume hay rations, occasionally supplemented with groundnut cake; while water and mineral salts were provided *ad lib*.

Collection of samples and evaluation: Following inoculation, the rectal temperatures and packed cell volumes (PCV), of the animals were monitored 3 times a week until *A. marginale* was detected microscopically. The PCV was determined using microhaematocrit method. Once *A. marginale* was detected, rectal temperature, determination of PCV

and degree of parasitaemia were carried out daily. The degree of parasitaemia was based on the percentage of parasitised cells out of 500 erythrocytes.

Treatment of the Clinical Disease: The animals were treated, individually, when the PCV dropped to 16% or below, using oxytetracycline at 10mg/kg. body weight intravenously (iv). A PCV of 16% or below was chosen because field observations have shown that most cases of clinical anaplasmosis are brought to the notice of clinicians at that point for treatment.

Three treatment regimens were followed. One group was treated once, the second group for 2 consecutive days and the third group for 3 consecutive days (iv).

Assessment of antibody response: Serum samples were regularly collected from all infected animals and tested for the presence of antibodies to *A. marginale*, using the rapid card agglutination test (Amerault and Roby, 1968; Amerault, 1973).

RESULTS

Clinical manifestation: Anaplasma bodies (*A. marginale*) were first detected microscopically in the intact calves between 16 and 23 days, while took between 23 and 33 days post-inoculation (pi), for them to be detected. The mean prepatent periods in intact and splenectomised calves were 20.9 and 25.2 respectively. The late appearance of Anaplasma bodies was not clear; since the contrary is more likely to occur. However, Figs 1 to 3 show the pattern of development of anaemia and parasitaemia in both splenectomised and intact animals given different treatment regimens.

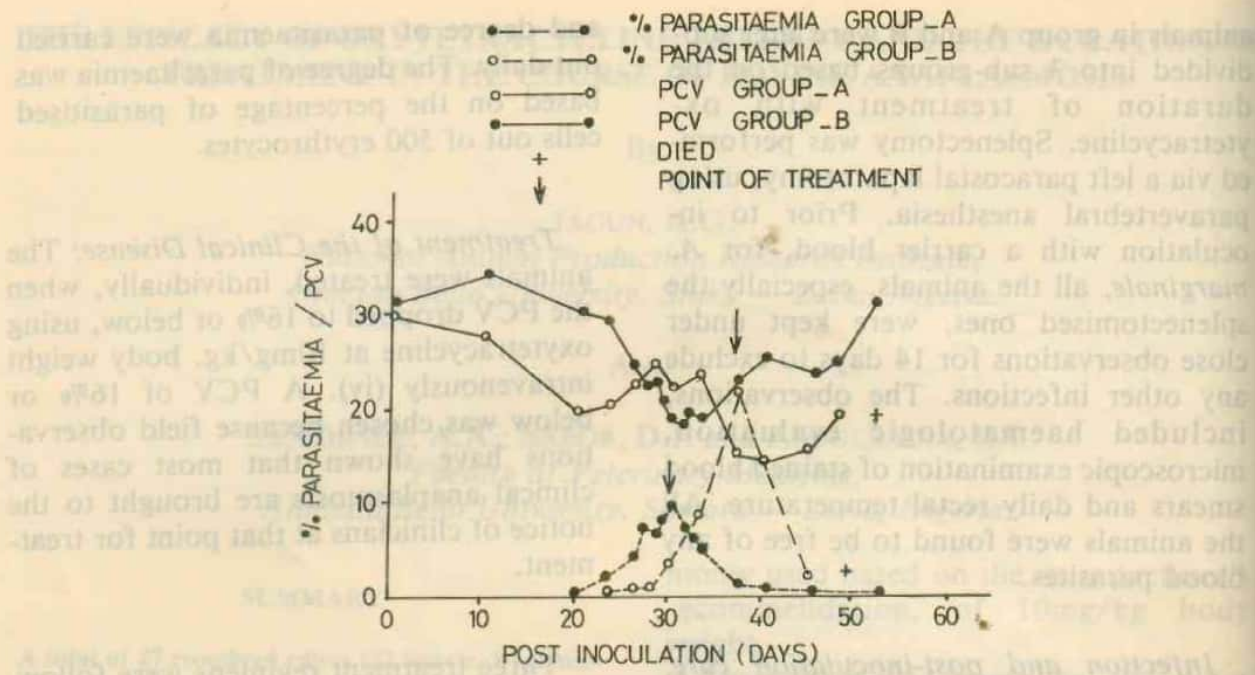


FIG-1 MEAN PARASITAEMIA AND PACKED CELL VOLUME (PCV) IN BOTH INFECTED INTACT (GROUP_A) AND SPLENECTOMISED (GROUP_B) ANIMALS TREATED ONCE WITH OXYTETRACYCLINE.

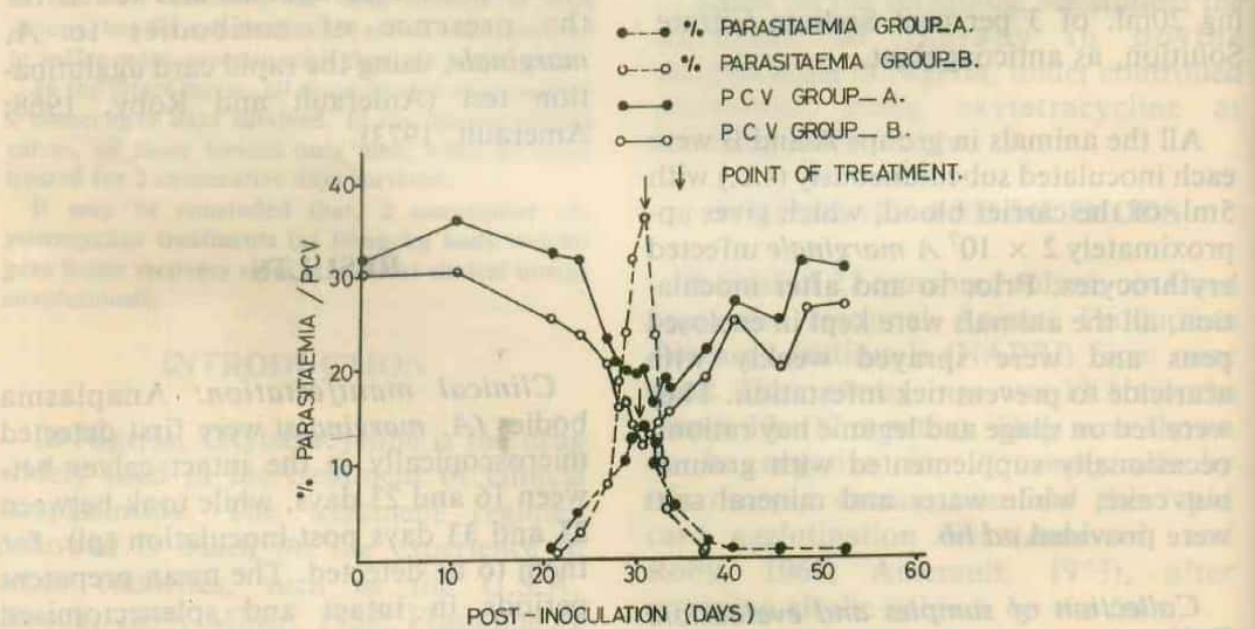


FIG-2 MEAN PARASITAEMIA AND PACKED CELL VOLUME (PCV) IN BOTH INFECTED INTACT (GROUP_A) AND SPLENECTOMISED (GROUP_B) ANIMALS TREATED TWICE WITH OXYTETRACYCLINE.

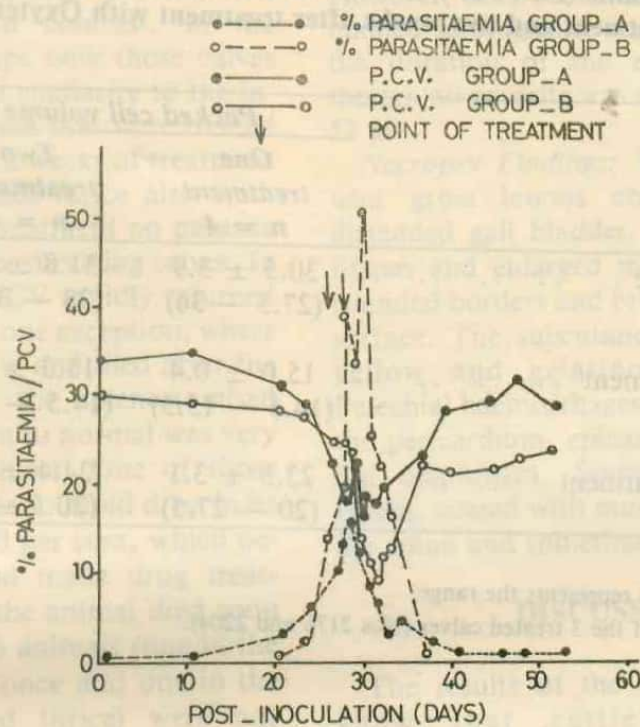


FIG-3 MEAN PARASITAEMIA AND PACKED CELL VOLUME (PCV) IN BOTH INFECTED INTACT (GROUP_A) AND SPLENECTOMISED (GROUP_B) ANIMALS TREATED THRICE WITH OXYTETRACYCLINE.

The pattern of parasitaemia, irrespective of whether treatment was given once, twice or thrice, appeared to be similar in both intact (group A) and splenectomised (group B) animals, except that the degree was more pronounced in group B. In group A, parasitaemia increased gradually from day 20 pi, until it was interrupted by therapy about day 30, when treatment was given. In group B, the parasitaemia increased so rapidly that it require earlier therapeutic intervention. The average of highest parasitaemia reached before treatment in group A and B were 13.26 and 35.41 per cent respectively.

The fluctuation in the PCV of the infected animals followed similar pattern. However, group B animals were observed to suffer more anaemic crisis than group A.

Tables I and II summarise the mean PCV values prior to exposure, at the time of treatment and 2 weeks after treatment in both intact (group A) and splenectomised (group B) animals. The average PCV values at the time of treatment were similar in each group. However, the average PCV values were very low in all the splenectomised calves at the time of

TABLE I

Packed cell volume (PCV) of intact calves (Group A) before inoculation, at point of treatment and two weeks after treatment with Oxytetracycline

	<i>Packed cell volume (Mean ± S.D)</i>		
	<i>One treatment</i> <i>n = 4</i>	<i>Two treatments</i> <i>n = 4</i>	<i>Three treatments</i> <i>n = 4</i>
Prior to exposure	30.5 ± 3.9 (27.5 — 36)	31.8 ± 2.3 (28 — 33.5)	33.2 ± 1.8 (31 — 35.5)
At point of treatment	15.0 ± 0.4 (14.5 — 15.5)	15.3 ± 0.8 (14.5 — 16.5)	15.2 ± 0.5 (14.5 — 15.5)
2 weeks after treatment	23.5 ± 3.1 (20 — 27.5)	24.4 ± 4.1 (20.5 — 29)	*27.5 ± 1.0 *(26.5 — 28.5)

Figure in parenthesis represents the range.

*Values for only 2 of the 3 treated calves (Nos 2176 and 2204).

TABLE II

Packed cell volume (PCV) of splenectomised calves (Group B) before inoculation, at point treatment and two weeks after treatment with Oxytetracycline

	<i>Packed cell volume (Mean ± S.D.)</i>		
	<i>One treatment</i> <i>n = 3</i>	<i>Two treatments</i> <i>n = 3</i>	<i>Three treatments</i> <i>n = 3</i>
Prior to exposure	30.2 ± 2.7 (26.5 — 33)	30.7 ± 2.1 (28 — 33)	29.8 ± 4.5 (25.5 — 36)
At point of treatment	13.5 ± 1.1 (12.5 — 15)	12.6 ± 1.0 (11.5 — 14)	11.5 ± 1.0 (10.5 — 12.5)
2 weeks after treatment	**	24.7 ± 3.0 (20.5 — 27.5)	(20.5)*

*PCV value for only one surviving calf (no 2195) at 2 weeks after treatment;

**All the calves died before 2 weeks of treatment.

Figure in parenthesis represents the range.

treatment (Table II). In the intact calves it was observed that 2 weeks after treatment the average PCV of all surviving animals had returned to almost pre-infection levels (Table I). In contrast, in the splenectomised groups only those calves treated twice showed similarity to the intact calves; while those that were treated once all died, before 2 weeks of treatment and 2 of those treated thrice also died. Beyond 14 days of treatment no parasite was detected in all the surviving calves. In the intact ones the PCV rapidly returned to normal, with only one exception, where it was persistently low and died after the third treatment. In the splenectomised calves the PCV return to normal was very gradual in the survivors. One of those treated thrice died due to rapid drop in its PCV from 18.5 to 10 per cent, which occurred overnight and made drug treatment less effective; the animal died soon after treatment. Two animals (one in the group to be treated once and one in the group to be treated thrice) were not treated as the PCV remained above 16 per cent.

In group B (i.e. Splenectomised) animals all those treated once died, while those treated twice all survived. However, 2 out of the 3 animals treated thrice died, because drug intervention was too late as the PCV drop was so rapid that by the time treatment was given the PCV values were 8.5 and 9 per cent respectively.

Serological response: The majority of the animals became serologically positive within 20 days of inoculation. By day 35 pi, all animals had become positive. The presence of detectable parasitaemia coincided with development of antibody response. Maximum serological response (+4) was not obtained early during the patent period until day 52 pi, in the majority of the animals. There was no difference in the response between intact and splenectomised animals, either in the degree of reaction or persistence of antibody within the period of the experiment. This observation agrees with the results reported by Jones *et al.* (1968 a, b)

using the complement fixation test; they observed similar pattern of response in both intact and splenectomised calves. However, in his study all the animals remained serologically positive throughout the duration of the experiment, even though no parasite was detected after day 52 pi.

Necropsy Findings: The most prominent gross lesions observed included, distended gall bladder, anaemic or pale tissues and enlarged mottled liver, with rounded borders and brownish-yellow cut surface. The subcutaneous tissue had a yellow and gelatinous appearance. Petechial haemorrhages were observed on the pericardium, epicardium, pleura and the diaphragm. Some had pellets or faeces, coated with mucus, were found in the colon and sometimes in the rectum.

DISCUSSION

The results of the experiment clearly show that cattle with clinical anaplasmosis (PCV 16%) could effectively be treated with oxytetracycline given on two consecutive days, at the rate of 10mg/kg body weight, without any adverse effect. However, it is not possible in this study to compare those with two treatments, with those that received three treatments, because of the unexpected mortalities recorded in the latter group. Nevertheless, since two treatments gave 100 per cent cure, it should be expected that if therapeutic intervention occurred early before severe anaemic crisis, as was observed in the animals that died in group 3, then 3 treatments should also result in complete cure with probably faster recovery period.

Although one treatment resulted in 100 per cent cure in intact calves, a similar result may not be expected in adult cattle so treated, since it has been shown by various workers (De kock and Quinlan 1962; Roby *et al.* 1961; Jones and Brock 1966; Jones *et al.* 1968 a,b) that young animals are less susceptible to *A. marginale* infection and have greater

ability to regenerate erythrocytes better than adults. This position is further supported by the finding of 100 per cent mortality in the splenectomised calves treated once. This then agrees with the fact that splenectomy overcomes innate resistance in infected calves and thus induces a situation similar to primary anaplasmosis in adult or aged cattle (De Kock and Quinlan, 1962; Roby *et al.* 1961; Jones and Borck, 1966). This does not mean that splenectomised animals are comparable in all respects with the adults, because the absence of the spleen does not make them immunologically incompetent. However, with 2 treatments, both intact and splenectomised calves were all cured of infection, suggesting that these could well be applicable to adult animals.

Although faster recovery was obtained in those intact animals treated thrice, it is unlikely that the difference in PCV, 2 weeks after treatment, justifies the additional expense. Taking the current market price of Oxytetracycline (Terramycin Q50 — Pfizer) as N0.019/kg; it will then require N11.64 to treat an average adult cattle, weighing 300kg, for 2 consecutive days, while it will cost N17.46 to treat the same animal for 3 consecutive days. It is, therefore, economical to give 2 consecutive treatments in clinical bovine anaplasmosis.

It is, also, evident from this study that for effective therapy in clinical anaplasmosis, treatment must be started as early as possible, preferably when the PCV is about 20 per cent or slightly below. Any delay may lead, not only to persistently low PCV and partial recovery, but death, when therapy is finally instituted. However, this does not mean that animals with clinical anaplasmosis and those with very low PCV may not survive when treated. This may require some supportive treatments, such as administration of blood transfusions (Jones and Norman, 1962; Franklin *et al.* 1962) or some haematinics (Brock *et al.* 1959), to enhance recovery rate. But more often than not, most supportive

treatments do not have time to stimulate erythropoiesis sufficiently enough to effect survival. For example, blood transfusion as an adjuvant to therapy induces recrudescence of the parasitaemia and its benefit has been questioned (Jones and Norman, 1962). Haematinics, on the other hand, are believed to reduce the time required for convalescence (Brock *et al.* 1959). From this study, it is apparent that 2 treatments of Oxytetracycline, at 10mg/kg body weight (iv) for 2 consecutive days are best to cure clinical bovine anaplasmosis. This could not be said to give a hundred per cent cure; but from economic point of view, it is better than treating for 3 consecutive days.

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... of the most important factors affecting the improvement in livestock production is the availability of cheap and good quality feedstuffs. As population increases faster than food production, expansion of existing methods of producing plant and animal protein will not meet the growing needs.

INTRODUCTION

In Nigeria, one of the major problems confronted by the poultry industry is the shortage of local feeds. The existing practice of heavy dependence on imported feed ingredients will continue to pose a constraint to the development of the livestock industry. One local source that could partially remedy this shortage is cassava (Manihot esculenta, Crantz).

Cassava is of great importance in the national economy of Nigeria and is second only to yam in total root production. Umanah (1976) projected that by 1985, Nigeria would be producing 13.9 million metric tons of cassava annually. Although the carbohydrate production exceeds that of other crops, early findings have shown that cassava root meal is not satisfactory replacement for maize in broiler chicks (Voor (1976) for example reported that growth depression was observed when 20